

**REMARKS**

Claims 1-19 were pending in the application at the time the final Office Action (the "Office Action") was mailed June 25, 2007, and at the time the Notice of Panel Decision from Pre-Appeal Brief Review was mailed on October 31, 2007. Claims 1, 3, 12-15 have been amended, claims 2, 4, and 7 have been canceled, and no claims have been added. Therefore, claims 1, 3, 5, 6, and 8-19 are now pending. No new matter has been added by virtue of this amendment and entry is respectfully requested. Support for the amendments to claim 1 can be found, for example, in Examples 1 and 2 ("under conditions that result in increased sperm motility") and on page 6, line 19 through line 2, page 7 ("wherein the sperm having increased motility can be used to impregnate a female subject").

***Claim Rejections Under 35 U.S.C. § 102***

Claims 1, 2, 5, 6, and 8-19 were rejected under 35 U.S.C. § 102(b) as being anticipated by Alexander et al (US 6,180,355 B1). Independent claim 1, from which all pending claims depend, has been amended herein to recite:

A method comprising the steps of:

a) providing from an infertile male subject having a spinal cord injury a biological sample comprising sperm and at least one cytokine selected from the group consisting of TNF $\alpha$ , IL1 $\beta$ , and IL6; and

b) contacting the biological sample in vitro with an agent that inactivates or reduces the biological activity of the at least one cytokine under conditions that result in increased sperm motility, wherein the sperm having increased motility can be used to impregnate a female subject.

Because Alexander et al. does not teach providing a biological sample from an infertile male having a spinal cord injury (SCI), or step b) of claim 1 as amended herein that results in sperm having increased motility that can be used to impregnate a female, claim 1 and the claims that depend therefrom are not anticipated by this reference.

Accordingly, withdrawal of this rejection is respectfully requested.

***Claim Rejections Under 35 U.S.C. § 103***

Claims 1, 2, 5, 6, and 8-19 were rejected under 35 U.S.C. 103(a) as being unpatentable over Alexander et al (US 6,180,355 BI) in view of Gruschwitz et al (*Journal of Andrology* 1996) and Angelopoulos et al (*Fertility and Sterility* 1999). Claims 3 and 4 were rejected under 103(a) as being unpatentable over Alexander et al., Gruschwitz et al., and Angelopoulos et al., and further in view of Brackett et al (*Physical Therapy* 1996). Claim 7 was rejected under 103(a) as being unpatentable over Alexander et al., Gruschwitz et al., and Angelopoulos et al., and further in view of Gerris. Claim 2 has been canceled. Independent claim 1, from which all pending claims depend, has been amended herein to recite:

A method comprising the steps of:

a) providing from an infertile male subject having a spinal cord injury a biological sample comprising sperm and at least one cytokine selected from the group consisting of TNF $\alpha$ , IL1 $\beta$ , and IL6; and

b) contacting the biological sample in vitro with an agent that inactivates or reduces the biological activity of the at least one cytokine under conditions that result in increased sperm motility, wherein the sperm having increased motility can be used to impregnate a female subject.

Claim 1 (and claims 5, 6, and 8-19 which depend therefrom) as amended herein is patentable over the combinations of 1) Alexander et al., Gruschwitz et al., and Angelopoulos et al.; 2) Alexander et al., Gruschwitz et al., Angelopoulos et al., and Brackett et al.; and 3) Alexander et al., Gruschwitz et al., Angelopoulos et al., and Gerris because none of these combinations yield a *prima facie* case of obviousness as there is no suggestion or motivation to combine or modify the references to arrive at the claimed invention.

Alexander et al. neither teaches nor discloses a method of increasing sperm motility, and certainly does not teach or suggest treating infertility by contacting a semen sample that contains

cytokines with an agent that inactivates or reduces the activity of the cytokines. Alexander et al. fails to even mention infertility and SCI. Instead, Alexander et al. discusses using generally available techniques of analysis of cytokines to diagnose and treat "Chronic Pelvic Pain Syndrome (CPPS)" or non-bacterial prostatitis. Alexander also discusses systemic steroid therapy, and in no way teaches or discloses the *in vitro* treatment of biological specimens containing sperm for use in impregnating a female, as taught by Applicants. Combining Gruschwitz and Angelopoulos et al. with Alexander et al. does not result in the instant invention. Gruschwitz et al. fails to even mention SCI, and instead teaches a correlation between cytokine content and the presence of a urogenital tract infection. Systemic administration of a steroid to men having CPPS as taught by Alexander et al. based on the correlation between urogenital tract infection and cytokine content as taught by Gruschwitz et al. would not result in the claimed invention.

Angelopoulos et al., does not cure the deficiencies of Alexander et al. in view of Gruschwitz. Angelopoulos et al. fails to even mention SCI, but instead describes different techniques of culturing testicular tissue and the subsequent effects on sperm motility. Angelopoulos et al. does not disclose or even suggest that cytokines in the seminal plasma cause poor motility in sperm or that affecting the behavior or activity of these cytokines *in vitro* will improve sperm motility. Thus, treating an infertile patient who has a SCI with a systemic administration of anticytokine agents as taught by Alexander et al., in view of Gruschwitz which discusses an anti-inflammatory response in a urogenital infection, and further in view of Angelopoulos et al. which discusses the effects of different culturing techniques on sperm motility, would still not result in the instant invention. The patient's infertility would not be addressed or changed by following these references. (See, also for example, the 37 C.F.R. § 1.132 Declarations of record).

Thus, this combination of references, all of which fail to mention or suggest obtaining a biological sample from a man having a SCI, does not render obvious a method of "providing from an infertile male subject having a spinal cord injury a biological sample comprising sperm and at least one cytokine selected from the group consisting of TNF $\alpha$ , IL1 $\beta$ , and IL6; and b) contacting the biological sample *in vitro* with an agent that inactivates or reduces the biological activity of the at

least one cytokine under conditions that result in increased sperm motility, wherein the sperm having increased motility can be used to impregnate a female subject", because none of these references, nor the combination thereof, teaches or suggests treating sperm *in vitro* from infertile men having a SCI with an agent that inactivates or reduces the biological activity of a cytokine that results in sperm having increased motility that can be used to impregnate a female.

Regarding the combination of Alexander et al., Gruschwitz et al., Angelopoulos et al., and Brackett et al., the deficiencies of the combination of Alexander et al., Gruschwitz et al., and Angelopoulos et al. are not cured by Brackett et al. This reference does not mention cytokines, and therefore does not teach or disclose that sperm in a biological sample can be made more motile by treating them with an agent that inactivates or reduces the biological activity of a cytokine in the sample. Brackett et al. does not suggest to one of skill in the art having possession of Alexander et al., Gruschwitz et al., and Angelopoulos et al. that the manipulation of cytokines in semen from men with a SCI would lead to sperm having increased motility for use in impregnating a female.

With regard to the combination of Alexander et al., Gruschwitz et al., Angelopoulos et al., and Gerris, the failure of the combination of Alexander et al., Gruschwitz et al., and Angelopoulos et al. to result in the claimed invention was discussed above. Gerris fails to cure the deficiencies of the combination of Alexander et al., Gruschwitz et al., and Angelopoulos et al. because Gerris describes sperm retrieval from the vagina as an alternative to masturbation. Gerris provides no mention of obtaining a biological sample from an infertile man having a SCI, and no mention of cytokines in semen. The vaginal sperm-retrieval methods of Gerris would not motivate or lead one of skill in the art who has considered Alexander et al., Gruschwitz et al., and Angelopoulos et al. to conceive of a method of "providing from an infertile male subject having a spinal cord injury a biological sample comprising sperm and at least one cytokine selected from the group consisting of TNF $\alpha$ , IL1 $\beta$ , and IL6; and b) contacting the biological sample *in vitro* with an agent that inactivates or reduces the biological activity of the at least one cytokine under conditions that result in increased sperm motility, wherein the sperm having increased motility can be used to impregnate a female subject."

In re Application of: Brackett N. L., et al.  
Confirmation No: 6890  
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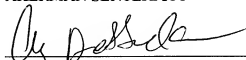
Based on the foregoing, applicants submit that the cited references, alone or in combination, do not render the claims as amended herein obvious within the meaning of 35 U.S.C. 103. The combinations of 1) Alexander et al., Gruschwitz et al., and Angelopoulos et al.; 2) Alexander et al., Gruschwitz et al., Angelopoulos et al., and Brackett et al.; and 3) Alexander et al., Gruschwitz et al., Angelopoulos et al., and Gerris all fail to provide a suggestion or motivation to combine or modify the references to arrive at the claimed invention.

Accordingly, withdrawal of these rejections is respectfully requested.

### CONCLUSION

It is believed that all claims are now in condition for immediate allowance. However, the Examiner is invited to call the undersigned (direct line: 561-671-3623) if it is believed that a telephonic interview would expedite the prosecution of the application to allowance. This amendment is being filed with an RCE and a petition for a one month extension of time and the required fees. Although Applicants believe that no further extensions of time are required with submission of this paper, Applicants request that this submission also be considered as a petition for any further extensions of time if necessary. The Commissioner for Patents and Trademarks is hereby authorized to charge the amount due for any retroactive extensions of time and any deficiency in any fees due with the filing of this paper or credit any overpayment in any fees paid on the filing or during prosecution of this application to Deposit Account No. 50-0951.

Respectfully submitted,  
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